

Amendments To The Claims:

This listing of the claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1. (Previously Presented) A nucleic acid comprising at least one region coding for an enzyme activity involved in the biosynthesis of spinosyn.
2. (Previously Presented) The nucleic acid of Claim 1 comprising a single-stranded or double-stranded DNA or RNA.
3. (Previously Presented) The nucleic acid of Claim 2 comprising a DNA fragment.
4. (Previously Presented) The nucleic acid of Claim 3 comprising all regions coding for enzyme activities which are involved in biosynthesis of spinosyn.
5. (Previously Presented) The nucleic acid of Claim 1 wherein said enzyme activity is selected from the group consisting of polyketide synthase, methyltransferase, glycosyltransferase, epimerase, aminotransferase, dimethyltransferase, reductase, dehydratase and cyclization enzyme.

Claim 6. (Canceled)

7. (Previously Presented) A nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, comprising at least one sequence selected from
 - (a) SEQ ID NO 1, 2, 3, 4, 5, 6, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 52 or 54,

- (b) a part sequence which is at least 14 base pairs in length of the sequences defined in (a),
 - (c) a sequence which hybridizes to a sequence defined in (a),
 - (d) a sequence which is at least 70% identical to a sequence defined in (a),
 - (e) a sequence which is complementary to a sequence defined in (a), and
 - (g) a sequence which, due to the degeneracy of the genetic code, codes for the same amino acid sequence as a sequence defined in (a) to (d).
8. (Previously Presented) The nucleic acid of Claim 7 comprising a sequence according to SEQ ID NOS: 1 to 6.
9. (Previously Presented) The nucleic acid of Claim 7 comprising a sequence according to SEQ ID NO: 4.
10. (Previously Presented) The nucleic acid of Claim 7 comprising a sequence according to SEQ ID NOS: 5 and 6.
11. (Previously Presented) The nucleic acid of Claim 7 comprising at least one sequence according to SEQ ID NOS: 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 or 39.
12. (Previously Presented) The nucleic acid of Claim 7 comprising at least one sequence according to SEQ ID NOS: 41, 43, 45, 47 or 49.
13. (Previously Presented) A regulatory region, which controls transcription of a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn in *Saccharopolyspora spinosa*.

14. (Previously Presented) A DNA construct comprising a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn and at least one heterologous promoter.
15. (Previously Presented) A vector comprising at least one nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, a regulatory region which controls transcription of said nucleic acid or a DNA construct comprising said nucleic acid and at least one heterologous promoter.
16. (Previously Presented) The vector of Claim 15, wherein the nucleic acid is functionally linked to regulatory sequences which ensure expression of the coding regions of the nucleic acid in prokaryotic or eukaryotic cells.
17. (Previously Presented) The vector of Claim 15 comprised of a BAC vector, PAC vector or a vector functionally equivalent to BAC or PAC vectors.
18. (Previously Presented) The vector of Claim 17 selected from the BAC clones having the deposition numbers DSM 13010, DSM 13011 and DSM 13012.
19. (Previously Presented) The vector of Claim 15 comprising a shuttle vector which can be transferred to prokaryotes and to eukaryotes.
20. (Previously Presented) The vector of Claim 15 comprising a shuttle vector which can be transferred to Gram-negative bacteria, Gram-positive bacteria and Archea.
21. (Previously Presented) The vector of Claim 15 comprising a shuttle vector which can be transferred to *Escherichia coli* and to actinomycetes.
22. (Previously Presented) The vector of Claim 21 comprising a shuttle vector which can be transferred to *Escherichia coli* and to *Streptomyces*.

23. (Previously Presented) The vector of Claim 15 which can be replicated autonomously in a prokaryote.
24. (Previously Presented) The vector of Claim 15 which can be integrated into the genome of a prokaryote via the phage Φ C31 integration mechanism, the pSAM2 integration mechanism or the mini-circle integration mechanism.
25. (Previously Presented) The vector of Claim 15 which can be integrated into the genome of a prokaryote by RecA-mediated recombination.
26. (Previously Presented) The vector of Claim 15 which can be integrated into the genome of a prokaryote by RecE- and RecT-mediated recombination.
27. (Previously Presented) A host cell comprising a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, a regulatory region which controls transcription of said nucleic acid, a DNA construct comprising said nucleic acid and at least one heterologous promoter or a vector comprising said nucleic acid, said regulatory region or said DNA construct.
28. (Previously Presented) The host cell of Claim 27 comprising a prokaryotic or eukaryotic cell.
29. (Previously Presented) The host cell of Claim 28, wherein the prokaryotic cell belongs to the group of actinomycetes.
30. (Previously Presented) The host cell of Claim 28, wherein the eukaryotic cell is a plant cell.
31. (Previously Presented) A polypeptide encoded by a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn.

32. (Previously Presented) The polypeptide of Claim 31 having a methyltransferase activity.
33. (Previously Presented) The polypeptide of Claim 32 comprising the amino acid sequence according to SEQ ID NOS: 8, 12, 14, 18 or 20, or a part sequence thereof.
34. (Previously Presented) The polypeptide of Claim 31 having a glycosyltransferase activity.
35. (Previously Presented) The polypeptide of Claim 34 comprising the amino acid sequence according to SEQ ID NOS: 10 or 30, or a part sequence thereof.
36. (Previously Presented) The polypeptide of Claim 31 having the activity of a C-C linking enzyme which carries out cyclization reactions.
37. (Previously Presented) The polypeptide of Claim 36 comprising the amino acid sequence according to SEQ ID NO: 16 or a part sequence thereof.
38. (Previously Presented) The polypeptide of Claim 31 having the activity of an enzyme which is involved in cyclization reactions.
39. (Previously Presented) The polypeptide of Claim 38 comprising the amino acid sequence according to SEQ ID NO: 22 or a part sequence thereof.
40. (Previously Presented) The polypeptide of Claim 31 having a 2,3-reductase activity.
41. (Previously Presented) The polypeptide of Claim 40 comprising the amino acid sequence according to SEQ ID NO: 24 or a part sequence thereof.
42. (Previously Presented) The polypeptide of Claim 31 having a 2,3-dehydratase activity.

43. (Previously Presented) The polypeptide of Claim 42 comprising the amino acid sequence according to SEQ ID NO: 26 or a part sequence thereof.
44. (Previously Presented) The polypeptide of Claim 31 having a thioesterase activity.
45. (Previously Presented) The polypeptide of Claim 44 comprising the amino acid sequence according to SEQ ID NO: 28 or a part sequence thereof.
46. (Previously Presented) The polypeptide of Claim 31 having a 3,4-dehydratase activity.
47. (Previously Presented) The polypeptide of Claim 46 comprising the amino acid sequence according to SEQ ID NO: 32 or a part sequence thereof.
48. (Previously Presented) The polypeptide of Claim 31 having a 4-aminotransferase activity.
49. (Previously Presented) The polypeptide of Claim 48 comprising the amino acid sequence according to SEQ ID NO: 34 or a part sequence thereof.
50. (Previously Presented) The polypeptide of Claim 31 having an N-dimethyltransferase activity.
51. (Previously Presented) The polypeptide of Claim 50 comprising the amino acid sequence according to SEQ ID NO: 36 or a part sequence thereof.
52. (Previously Presented) The polypeptide of Claim 31 having a 3,4-reductase activity.
53. (Previously Presented) The polypeptide of Claim 52 comprising the amino acid sequence according to SEQ ID NO: 38 or a part sequence thereof.

54. (Previously Presented) The polypeptide of Claim 31 having a transcription regulator activity.
55. (Previously Presented) The polypeptide of Claim 54 comprising the amino acid sequence according to SEQ ID NO: 40 or a part sequence thereof.
56. (Previously Presented) The polypeptide of Claim 31 having a polyketide synthase activity.
57. (Previously Presented) The polypeptide of Claim 56 comprising the amino acid sequence according to SEQ ID NOS: 42, 44, 46, 48 or 50, or a part sequence thereof.
58. (Previously Presented) The polypeptide of Claim 31 having a glucose dehydratase activity.
59. (Previously Presented) The polypeptide of Claim 58 comprising the amino acid sequence according to SEQ ID NO: 53.
60. (Previously Presented) The polypeptide of Claim 31 having a 3,5-epimerase activity.
61. (Previously Presented) The polypeptide of Claim 60 comprising the amino acid sequence according to SEQ ID NO: 55.
62. (Previously Presented) An enzyme involved in a cyclization reaction, comprising the amino acid sequence according to SEQ ID NO: 15 or 22 or a part sequence thereof which is able to carry out at least part of said reaction or has an amino acid sequence at least 50% identical thereto.
63. (Previously Presented) An antibody, which reacts specifically with a polypeptide of Claim 31.

64. (Previously Presented) A method for preparing a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, said method comprising:

synthesizing the complete nucleic acid by chemical methods or
synthesizing oligonucleotides by chemical methods,
labelling said oligonucleotides,
hybridizing said oligonucleotides to DNA of a genomic or
cDNA library which has been prepared from genomic
DNA or mRNA from *S. spinosa*,
selecting positive clones and
isolating the hybridizing DNA from positive clones or

synthesizing oligonucleotides by chemical methods and
amplifying the target DNA by PCR.

65. (Previously Presented) Method for preparing a polypeptide encoded by a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, said method comprising:

culturing a host cell comprising said nucleic acid, a regulatory region which controls transcription of said nucleic acid, a DNA construct comprising said nucleic acid and at least one heterologous promoter or a vector comprising said nucleic acid, said regulatory region or said DNA construct under conditions which ensure expression of said nucleic acid, or

expressing said nucleic acid in an *in vitro* system, and

obtaining the polypeptide from the cell, the culture medium or the *in vitro* system.

66. (Previously Presented) A method for preparing spinosyn, spinosyn precursors or spinosyn derivatives, comprising:

culturing a host cell comprising a nucleic acid comprised of at least one region which codes for an enzyme activity involved in the biosynthesis of spinosyn, a regulatory region which controls transcription of said nucleic acid, a DNA construct comprising said nucleic acid and at least one heterologous promoter or a vector comprising said nucleic acid, said regulatory region or said DNA construct under conditions which ensure expression of said nucleic acid, and

obtaining the spinosyn, spinosyn precursor or spinosyn derivative from the cell or the culture medium.

67. (Previously Presented) A method for preparing spinosyn derivatives, including spinosyn precursors, comprising:

exchanging at least one module-encoding nucleic acid sequence according to Claim 7 for at least one other module-encoding nucleic acid sequence according to Claim 7, or

exchanging at least one module-encoding nucleic acid sequence according to Claim 7 for at least one other module-encoding nucleic acid sequence from *S. spinosa*, or

exchanging at least one module-encoding nucleic acid sequence according to Claim 7 for at least one other module-encoding nucleic acid sequence from an organism other than *S. spinosa*, or

exchanging at least one domain-encoding nucleic acid sequence according to Claim 7 for at least one other domain-encoding nucleic acid sequence according to Claim 7, or

exchanging at least one domain-encoding nucleic acid sequence according to Claim 7 for at least one other domain-encoding nucleic acid sequence from *S. spinosa*, or

exchanging at least one domain-encoding nucleic acid sequence according to Claim 7 for at least one other domain-encoding nucleic acid sequence from an organism other than *S. spinosa*, or

exchanging a first acyltransferase-encoding nucleic acid sequence according to Claim 7 for a second acyltransferase-encoding nucleic acid sequence according to Claim 7, wherein the second acyltransferase has a substrate specificity different from that of the first acyltransferase, or

exchanging a first acyltransferase-encoding nucleic acid sequence according to Claim 7 for a second acyltransferase-encoding nucleic acid sequence from *S. spinosa*, wherein the second acyltransferase has a substrate specificity different from that of the first acyltransferase, or

exchanging a first acyltransferase-encoding nucleic acid sequence according to Claim 7 for a second acyltransferase-encoding nucleic acid sequence from an organism other than *S. spinosa*, wherein the second acyltransferase has a substrate specificity different from that of the first acyltransferase, or

deleting at least one domain-encoding nucleic acid sequence according to Claim 7, or

integrating at least one domain-encoding nucleic acid sequence according to Claim 7 into a module-encoding nucleic acid sequence according to Claim 7, or

mutating at least one domain-encoding nucleic acid sequence according to Claim 7,
and expressing the recombinant nucleic acid sequence in a host cell under conditions which allow synthesis of a spinosyn derivative or a spinosyn precursor.

Claims 68-69. (Canceled)

70. (Previously Presented) A method for attaching a forosamine sugar residue to the spinosyn aglycone or to the spinosyn 17-pseudoaglycone or to a polyketide aglycone, said method comprising:

transferring a nucleic acid according to SEQ ID NOS: 23, 25, 29, 31, 33, 35 and 37 into a host cell which can produce the spinosyn aglycone or the spinosyn 17-pseudoaglycone or the polyketide aglycone, or

transferring a nucleic acid according to SEQ ID NOS: 23, 25, 29, 31, 33, 35 and 37 into a host cell which cannot produce the spinosyn aglycone or the spinosyn 17-pseudoaglycone or the polyketide aglycone and adding the spinosyn aglycone or the spinosyn 17-pseudoaglycone or the polyketide aglycone to the culture medium, and

culturing the host cell under conditions which lead to an active cell metabolism.

71. (Previously Presented) A method for attaching a trimethylrhamnose sugar residue to the spinosyn aglycone or the spinosyn 9-pseudoaglycone or to a polyketide aglycone, said method comprising:

transferring a nucleic acid according to SEQ ID NO: 7, 9, 11, 13, 17 and/or 19 into a host cell which can produce the spinosyn aglycone or the spinosyn 9-pseudoaglycone or the polyketide aglycone, or

transferring a nucleic acid according to SEQ ID NO: 7, 9, 11, 13, 17 and/or 19 into a host cell which cannot produce the spinosyn aglycone or the spinosyn 9-pseudoaglycone or the polyketide aglycone and adding the spinosyn aglycone or the spinosyn 9-pseudoaglycone or the polyketide aglycone to the culture medium, and

culturing the host cell under conditions which lead to an active cell metabolism.

72. (Previously Presented) The method of Claim 71, wherein nucleic acids according to SEQ ID NOS: 9, 11, 13 and 17 are transferred.
73. (New) A vector for heterologous expression of a gene cluster for spinosyn biosynthesis, comprising nucleic acids that code for enzymes involved in the biosynthesis of spinosyn.
74. (New) The vector of Claim 73, wherein the vector is comprised of a BAC vector, a PAC vector or a vector functionally equivalent to BAC or PAC vectors.
75. (New) The vector of Claim 73, wherein the vector comprises a shuttle vector which can be transferred to prokaryotes and to eukaryotes.
76. (New) The vector of Claim 73, wherein the vector comprises a shuttle vector which can be transferred to Gram-negative bacteria, Gram-positive bacteria and Archea.
77. (New) The vector of Claim 73, wherein the vector comprises a shuttle vector which can be transferred to Escherichia coli and to actinomycetes.
78. (New) The vector of Claim 73, wherein the vector comprises a shuttle vector which can be transferred to Escherichia coli and to Streptomyces.

79. (New) The vector of Claim 73, wherein the vector can be replicated autonomously in a prokaryote.
80. (New) The vector of Claim 73, wherein the vector can be integrated into the genome of a prokaryote via the phage Φ C31 integration mechanism, the pSAM2 integration mechanism or the mini-circle integration mechanism.
81. (New) The vector of Claim 73, wherein the vector can be integrated into the genome of a prokaryote by RecA-mediated recombination.
82. (New) The vector of Claim 73, wherein the vector can be integrated into the genome of a prokaryote by RecE- and RecT-mediated recombination.
83. (New) A host cell comprising the vector of Claim 73.
84. (New) The host cell of Claim 83, wherein the host cell comprises a prokaryotic or eukaryotic cell.
85. (New) The host cell of Claim 84, wherein the prokaryotic cell belongs to the group of actinomycetes.
86. (New) The host cell of Claim 84, wherein the eukaryotic cell is a plant cell.
87. (New) A method for preparing spinosyn, comprising:
 - a) culturing the host cell of Claim 83, or
 - b) expressing said nucleic acids that code for the enzymes involved in the biosynthesis of spinosyn in an in vitro system; and
 - c) obtaining the spinosyn from the host cell or the in vitro system.

ELECTION

The Examiner has required restriction under 35 U.S.C. §§ 121 and 372 as follows:

SuperGroup A (Groups 1-69), claims 1-12, 14-30 and 65, drawn to nucleic acids coding for an enzyme activity, one of 69, involved in spinosyn biosynthesis.

Group 70, claim 13, drawn to a regulatory region from *S. spinosa*.

SuperGroup B (Groups 71-140), claims 31-62, drawn to polypeptides involved in spinosyn biosynthesis.

SuperGroup C (Groups 141-210), claim 63, drawn to antibodies specific for polypeptides involved in spinosyn biosynthesis.

SuperGroup D (Groups 211-280), claim 64, drawn to methods of making nucleic acids coding for an enzyme activity, one of 69, involved in spinosyn biosynthesis.

SuperGroup E (Groups 281-350), claims 66-67, drawn to methods of making spinosyn-like compounds using nucleic acids coding for enzymatic activity, one of 69, involved in spinosyn biosynthesis.

Group 351, claim 70, drawn to methods of glycosylating a spinosyn using SEQ ID Nos:23, 25, 29, 31, 33, 35 and 37 (using all 7 nucleic acid sequences).

SuperGroup F (Groups 352-357), claims 71 and 72, drawn to methods of glycosylating a spinosyn using particular nucleic acids involved in spinosyn biosynthesis.

Applicant hereby elects for further prosecution the invention of SuperGroup A, Group 1 (claims 1-12, 14-30 and 65) with traverse.

Applicant has added new claims 73-87 which should also be examined with Group 1. Thus, claims 1-12, 14-30, 65 and 73-87 are elected should the Restriction Requirement be maintained.